CLAIMS

We claim:

1. A biodegradable polymeric system possessing reverse thermal gelation properties comprising a mixture of at least a Component I triblock copolymer and a Component II triblock copolymer, said triblock copolymers comprising biodegradable polyester A-polymer blocks and polyethylene glycol B-polymer blocks, wherein the B-polymer block of said Component I triblock copolymer has an average molecular weight of 900 to 2000 Daltons and the B-polymer block of said Component II triblock copolymer has an average molecular weight of 600 to 2000 Daltons, and wherein said Component I triblock copolymer has an average molecular weight of between 2500 to 8000 Daltons and said component II triblock copolymer has an average molecular weight of between 800-7200 Daltons.

2. The biodegradable polymeric system according to Claim 1 wherein an aqueous solution of said Component I triblock copolymer has a lower gelation temperature than an aqueous solution of said Component II triblock copolymer.

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3. The biodegradable polymeric system according to Claim 1 wherein the biodegradable polyester A-polymer block is synthesized from monomers selected from the group consisting of D,L-lactide, D-lactide, L-lactide, D,L-lactic acid, D-lactic acid, L-lactic acid, glycolide, glycolic acid, ϵ-caprolactone, ϵ-hydroxyhexanoic acid, γ-butyrolactone, γ-hydroxybutyric acid, δ-valerolactone, δ-hydroxyvaleric acid, hydroxybutyric acids, malic acid, and copolymers thereof.

4. The biodegradable polymeric system according to Claim 1 wherein Component I and Component II triblock copolymers are selected from the group consisting of ABA and BAB type copolymers and mixtures thereof.

5. The biodegradable polymeric system according to Claim 4 wherein the Component I and Component II triblock copolymers are each of the BAB type.

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6. The biodegradable polymeric system according to Claim 4 wherein the Component I and Component II triblock copolymers are each of the ABA type.

7. The biodegradable polymeric system according to Claim 4 wherein the Component I triblock copolymer is an ABA type and the Component II triblock copolymer is a BAB type.

8. The biodegradable polymeric system according to Claim 4 wherein the Component I triblock copolymer is a BAB type and the Component II triblock copolymer is an ABA type.

9. The biodegradable polymeric system according to Claim 3 wherein the A-polymer block is a biodegradable polyester synthesized from monomers selected from the group consisting of D,L-lactide, D-lactide, L-lactide, D,L-lactic acid, D-lactic acid, L-lactic acid, glycolide, glycolic acid, ϵ-caprolactone, ϵ-hydroxyhexanoic acid, and copolymers thereof.

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10. The biodegradable polymeric system according to Claim 9 wherein the biodegradable A-polymer block is poly(D,L-lactide-co-glycolide)(PLG) synthesized from monomers selected from the group consisting of D,L-lactide, D-lactide, L-lactide, D,L-lactic acid, D-lactic acid, L-lactic acid, glycolide, glycolic acid, and copolymers thereof.

11. The biodegradable polymeric system according to Claim 10 wherein the A-polymer block of each Component I and Component II tri-block copolymer has a mole ratio of lactide to glycolide in a range of between 3:1 to 1:0.

12. The biodegradable polymeric system according to Claim 11 wherein the A-polymer block of each Component I and Component II tri-block copolymer has a mole ratio of lactide to glycolide in a range of between 1:1 to 1:0.

13. The biodegradable polymeric system according to Claim 10 wherein the Component I triblock copolymer has A-polymer block/B-polymer block weight ratio between 1.3 to

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3.0 and the Component II triblock copolymer has A-polymer block/B-polymer block weight ratio between 0.37 to 2.6.

14. An aqueous biodegradable polymeric drug delivery composition possessing reverse thermal gelation properties comprised of an aqueous phase having uniformly contained therein:

(a) an effective amount of a drug; and

(b) a biodegradable polymeric system possessing reverse thermal gelation properties comprising a mixture of at least a Component I triblock copolymer and a Component II triblock copolymer, said triblock copolymers comprising biodegradable polyester A-polymer blocks and polyethylene glycol B-polymer blocks, wherein the B-polymer block of said Component I triblock copolymer has an average molecular weight of 900 to 2000 Daltons and the B-polymer block of said Component II triblock copolymer has an average molecular weight of 600 to 2000 Daltons, and wherein said Component I triblock copolymer has an average molecular weight of between 2500 to 8000 Daltons and said Component II triblock copolymer has an average molecular weight of between 800-7200 Daltons

15. The aqueous polymeric drug delivery composition according to Claim 14 wherein the biodegradable polymeric system content of said composition is between about 3 and 50% by weight.

16. The aqueous polymeric drug delivery composition according to Claim 14 wherein the drug content of said composition is between about 0.0001 and 30% by weight.

17. The aqueous polymeric drug delivery composition according to Claim 14 wherein said drug is a polypeptide or protein, gene, hormone, anti-cancer or anti-cell proliferation agent.

18. The aqueous polymeric drug delivery composition according to Claim 17 wherein said polypeptide or protein is a member selected from the group consisting of oxytocin, vasopressin, adrenocorticotropic hormone, epidermal growth factor, platelet-derived growth factor (PDGF), prolactin, luliberin, luteinizing hormone releasing hormone (LHRH),

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LHRH agonists, LHRH antagonists, growth hormone (human, porcine, bovine, etc.), growth hormone releasing factor, insulin, erythropoietin, somatostatin, glucagon, interleukin-2 (IL-2), interferon-(α, β, or γ), gastrin, tetragastrin, pentagastrin, urogastrone, secretin, calcitonin, enkephalins, endorphins, angiotensins, thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), macrophage-colony stimulating factor (M-CSF), heparinase, bone morphogenic protein (BMP), hANP, glucagon-like peptide (GLP-1), interleukin-11 (IL-11), renin, bradykinin, bacitracins, polymyxins, colistins, tyrocidine, gramicidins, cyclosporins and synthetic analogues, modifications and pharmacologically active fragments thereof, enzymes, cytokines, antibodies, tissue fragments and vaccines.

19. The aqueous polymeric drug delivery composition according to Claim 17 wherein said polypeptide is a

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hepatitis vaccine, or synthetic analogue, modification or pharmacologically active fragment thereof.

20. The aqueous polymeric drug delivery composition according to Claim 17 wherein said hormone is a member selected from the group consisting of testosterone, estradiol, progesterone, prostaglandins, and synthetic analogues, modifications and pharmaceutical equivalents thereof.

21. The aqueous polymeric drug delivery composition according to Claim 16 wherein said anti-cancer agent is a member selected from the group consisting of mitomycin, bleomycin, BCNU, carboplatin, doxorubicin, daunorubicin, methotrexate, paclitaxel, taxotere, actinomycin D, camptothecin, synthetic analogues, modifications and pharmaceutical equivalents thereof.

22. A method for the administration of a drug to a warm blooded animal in a controlled release form which comprises:

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(1) providing an aqueous biodegradable polymeric drug delivery composition possessing reverse thermal gelation properties comprised of an aqueous phase having uniformly contained therein:

(a) an effective amount of a drug; and

(b) a biodegradable polymeric system possessing reverse thermal gelation properties comprising a mixture of at least a Component I triblock copolymer and a Component II triblock copolymer, said triblock copolymers comprising biodegradable polyester A-polymer blocks and polyethylene glycol B-polymer blocks, wherein the B-polymer block of said Component I triblock copolymer has an average molecular weight of 900 to 2000 Daltons and the B-polymer block of said Component II triblock copolymer has an average molecular weight of 600 to 2000 Daltons, and wherein said Component I triblock copolymer has an average molecular weight of between 2500 to 8000 Daltons and said component II triblock copolymer has an average molecular weight of between 800-7200 Daltons;

(2) maintaining said composition as a liquid at a

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temperature below the gelation temperature of said biodegradable polymeric system; and

(3) administering said composition as a liquid to said warm blooded animal with the subsequent formation of a gel as the temperature of said composition is raised by the body temperature of said animal to be above the gelation temperature of the biodegradable polymeric system.

23. The method according to Claim 22 wherein said administration is by parenteral, ocular, topical, inhalation, transdermal, vaginal, buccal, transmucosal, transurethral, rectal, nasal, oral, pulmonary or aural means.

24. The method according to Claim 22 wherein the biodegradable polymeric system content of said composition is between about 3 and 50% by weight.

25. The method according to Claim 22 wherein the drug content of said composition is between about 0.0001 and 20% by weight.

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26. The method according to Claim 22 wherein said drug administered is a polypeptide or protein, gene, hormone, anti-cancer or anti-cell proliferation agent.

27. The method according to Claim 26 wherein said polypeptide or protein is a member selected from the group consisting of erythropoietin, oxytocin, vasopressin, adrenocorticotropic hormone, epidermal growth factor, platelet-derived growth factor (PDGF), prolactin, luliberin, luteinizing hormone releasing hormone (LHRH), LHRH agonists, LHRH antagonists, growth hormone (human, porcine, bovine, etc.), growth hormone releasing factor, insulin, somatostatin, glucagon, interleukin-2 (IL-2), interferon-(α, β or γ), gastrin, tetragastrin, pentagastrin, urogastrone, secretin, calcitonin, enkephalins, endorphins, angiotensins, thyrotropin releasing hormone (TRH), tumor necrosis factor (TNF), nerve growth factor (NGF), granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), macrophage-colony stimulating factor (M-CSF), heparinase, bone morphogenic protein (BMP), hANP, glucagon-like peptide (GLP-1), interleukin-11 (IL-11),

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renin, bradykinin, bacitracins, polymyxins, colistins, tyrocidine, gramicidins, cyclosporins and synthetic analogues, modifications and pharmacologically active fragments thereof, enzymes, cytokines, antibodies, tissue fragments and vaccines.

28. The method according to Claim 27 wherein said polypeptide is a hepatitis vaccine, synthetic analogue, modification or pharmacological active fragment thereof.

29. The method according to Claim 26 wherein said hormone is a member selected from the group consisting of testosterone, estradiol, progesterone, prostaglandins and synthetic analogues, modifications and pharmaceutical equivalents thereof.

30. The method according to Claim 26 wherein the anti-cancer agent selected from the group consisting of mitomycin, bleomycin, BCNU, carboplatin, doxorubicin, daunorubicin, methotrexate, paclitaxel, taxotere, actinomycin D, camptothecin, and synthetic analogues, modifications and pharmaceutically equivalents thereof.

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31. A process of preparing the biodegradable polymeric system of Claim 1 comprising mixing the different types tri-block copolymer components before polymerization in one reaction pot and then polymerizing the triblock copolymer mixtures.

32. The process of preparing the biodegradable polymeric system of Claim 1 comprising synthesizing the different types of triblock copolymer components separately, and then mixing them into a mixture of the components.

33. A biodegradable copolymer mixture made from the process of Claim 31.

34. A biodegradable copolymer mixture made from the process of Claim 32.

35. A method of adjusting the gelation properties of a biodegradable polymeric system without negatively affecting its gel quality by providing the biodegradable polymeric

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system of Claim 1, wherein the gelation temperature of the system is adjusted by selecting proper individual biodegradable triblock copolymer components.

36. The method according to Claim 35, wherein the individual triblock polymer component can be selected based on at least one member of the group consisting of average molecular weights of A-polymer block, average molecular weights of B-polymer block, weight ratios of A-polymer block over B-polymer block, and types of triblock copolymer.

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